

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of Georg BERGER, Andrea SPITZER,
Christian JAEGER, Jutta PAULI and
Renate GILDENHAAR

Confirmation No.: 4082

Application No.: 10/689,219

Examiner: AZPURU, Carlos A.

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Group Art Unit: 1615

Attorney Docket No.: 3975.026

Customer Number: 30448

For: BONE REPLACEMENT MATERIAL COMPRISING CRYSTALLINE AND X-
RAY AMORPHOUS PHASES

DECLARATION UNDER 37 C.F.R. §1.132 BY DR. G. M. BERGER

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Georg M. Berger, do declare:

1. I am a co-inventors of the subject matter claimed in the above-captioned application ("the Application").

2. I hold a first doctor's degree (Dr. Ing. / Doctor of Engineering Science), which I obtained in 1975 at the University of Architecture and Civil Engineering, Weimar, Germany, and a second doctor's degree (Dr. sc. techn. / Doctor of Science and Technology) obtained in 1986 at the former Academy of Science of the German Democratic Republic. Since 1975, I have been employed as a materials scientist conducting research in biomaterials and ceramics. My activities as a chemist during the last 32 years are characterized by about 160 publications and by

several other highlights, and for some of these highlights my employer decided to apply for national and/or international patents, in the field of implants and bone replacement materials. Some more recent examples include US 6,767,854; DE 101 29 842; DE 102 49 626; EP 1 395 300; EP 1 395 295; US 7 223 420; US 7,109,254, and others.

3. I have reviewed the non-final Office Action mailed November 23, 2007 (hereinafter "Office Action") and the assertions therein, as well as the cited references. In the Office Action, claims 1-16 and 20 are rejected under 35 U.S.C. § 103(a) as being obvious over WIPO Publication WO91/07357 filed by Berger *et al.* (hereinafter "Berger").

In the Office Action, the Examiner states that:

[Berger] sets out the same raw materials as claimed herein. Berger forms a crystalline and amorphous phase. Processing of the material appears to utilize heat melting of the materials. It is therefore the position of this examiner, that those of ordinary skill would have expected not only the same composition characteristics from the work up of these materials as taught by Berger et al, but also the same bone replacement effects.

Office Action, pages 2-3.

It is my understanding that in order to render the claims obvious, the reference must disclose or suggest both the desirability of the claimed composition and a method of creating the claimed composition. I am well acquainted with WO 91/07357, as it concerns another invention where I was the lead inventor. Based on the following discussion, it should become clear that Berger simply does not meet the necessary standard because Berger does not disclose or suggest either the necessary starting materials or the thermal treatment required to form the resulting crystal phases and inorganic compounds of the claimed invention.

It is well known in the art that the type of *crystalline phases and amorphous phases* and the relative amounts of each are directly linked to the starting materials and the melting and cooling process to which the starting materials are exposed. A factor of significant importance to the resulting crystalline and amorphous phases is the particular tempering steps to which the starting material is exposed.

Similarly, it is well known that the *specific inorganic compounds* formed during a heating and cooling process are directly linked to the hold points and maximum temperature reached during the thermal process. Instant claim 2 is a product-by-process claim reciting specific

conditions and starting materials for preparing the claimed powder mixture, which recites both specific inorganic compounds and specific crystalline and amorphous phases. *The conditions and starting materials set forth in claim 2 are the only method I am aware of for producing the mixture of crystalline and amorphous phases with the claimed mixture of orthophosphates, diphosphates, and, as in claim 3, chain phosphates.*

I am fluent in German and have reviewed the Berger publication. Claim 8 of Berger is drawn to a vitreous or vitreous-crystalline material manufactured by melting together a powder mixture of 20-55%-wt CaO, 5-25% Na₂O, 0-15% K₂O, 0-15% MgO, 30-50% P₂O₅, 0-15% SiO₂, 0-40% Na₂SO₄ and/or K₂SO₄. This mixture is melted together by heating the materials to 1200-1580°C for a period of at least 10 minutes. The Berger material then undergoes spontaneous cooling or temperature-controlled cooling. Finally, the Berger material may be treated with a tempering step at 600-1200°C during the cooling. The product produced by the method disclosed in Berger is completely different from the instant product with respect to the crystal phases and the inorganic compounds produced.

The Office Action indicated that the Berger rejection will not be withdrawn absent data that "shows that the same materials produce different NMR, X-Ray diffractometric measurements, and the X-Ray amorphous and crystal phases differ from what is currently claimed." In order to confirm that nonobvious differences exist between the Application and Berger, I am submitting Table 1, which provides a comparison of the raw materials, processing steps, and end properties of the materials produced by the Application and the Berger reference. Please note that the inorganic composition data in row 6 of Table 1 was obtained using X-Ray diffractometry and the diphosphate percentages in row 7 were obtained using ³¹P-NMR measurements. These are the same methods used to describe the bone replacement materials of the pending claims.

Comparison Table 1 – Comparing the process used in Berger (WO 91/07357) to that of claim 2.

Process	
U.S. Serial No. 10/689,219	Berger (WO 91/07357)
1. Melting together one powder mixture of CaO 28-33% P ₂ O ₅ 40-52% Na ₂ O 8.5-13% K ₂ O 9.5-15%	1. Melting together a powder mixture of CaO 20-55% P ₂ O ₅ 30-50% Na ₂ O 5-25% K ₂ O 0-15%

Process	
U.S. Serial No. 10/689,219	Berger (WO 91/07357)
MgO 1.5-3% SiO ₂ 1-4%	MgO 0-15% SiO ₂ 0-15% 0-40 wt-% Na ₂ SO ₄ and/or K ₂ SO ₄
2. Step-by-step heating with holds for tempering at: a) 350-450°C b) 750-850°C c) 950-1050°C	2. No tempering holds at heating
3. Melting temperature 1550-1650°C	3. Melting temperature 1200-1580°C
4. Spontaneous cooling or temperature-controlled cooling	4. Spontaneous cooling or temperature-controlled cooling
5. No holding steps during cooling	5. Optional holding step at 600-1200°C during the cooling
6. PRODUCT: A powder mixture of crystal phases Ca ₂ K _{1-X} Na _{1+X} (PO ₄) ₂ , Na ₂ CaP ₂ O ₇ , K ₂ CaP ₂ O ₇ , Ca ₂ P ₂ O ₇ and X-ray amorphous (non-crystal) phases.	6. PRODUCT: A glassy or glassy-crystal body with the phases rhenanite = CaNaPO ₄ phase X = Ca ₂ KNa(PO ₄) ₂ phase A = Ca ₅ Na ₂ (PO ₄) ₄ glaserite = K ₃ Na(SO ₄) ₂ crystalline potassium sulfate = K ₂ SO ₄ and their mixed crystals.
7. PRODUCT: 0.1-30 wt-% diphosphates	7. PRODUCT: 0% diphosphates
8. PRODUCT SOLUBILITY: 30-500 µg/mg (claim 13)	8. PRODUCT SOLUBILITY: 1-15 mg/g

The clearly distinguishable crystal phases and compositions in Berger and the claims of the Application result because of their divergent thermal history and the different starting materials. The starting materials in Berger include 0-40 wt-% Na₂SO₄ and/or K₂SO₄, whereas the current Application does not mention Na₂SO₄ or K₂SO₄, much less include either in the claims. The claimed bone replacement material is formed using a much narrower range of starting materials.

This divergent thermal history is clearly set forth for ease of comparison in rows 2 and 3 of Comparison Table 1, below, and the following summary:

- The claimed invention includes three holds (350-450°C, 750-850°C and 950-1,050°C) during the heating process, Berger discloses none.
- The claimed invention has a maximum heating temperature of 1550-1650°C, whereas

Berger's maximum heating temperature is 1200-1580°C.

- The claimed invention provides for spontaneous cooling or temperature-controlled cooling without any holding step, whereas Berger includes a holding step in the range of 600-1200°C.

Further evidence that the claimed bone replacement material is neither disclosed nor suggested by the Berger materials is demonstrated by the substantially different solubility exhibited by each (30-500µg/mg v. 1-15 mg/g).

As set forth in table 1, the process disclosed in Berger produces A glassy or glassy-crystal material with the following phases: rhenanite = CaNaPO_4 ; phase X = $\text{Ca}_2\text{KNa}(\text{PO}_4)_2$; phase A = $\text{Ca}_5\text{Na}_2(\text{PO}_4)_4$; glaserite = $\text{K}_3\text{Na}(\text{SO}_4)_2$; crystalline potassium sulfate = K_2SO_4 ; and their mixed crystals. The pending claims require 0.1 to 20 wt-% of $\text{Na}_2\text{CaP}_2\text{O}_7$, $\text{K}_2\text{CaP}_2\text{O}_7$, $\text{Ca}_2\text{P}_2\text{O}_7$, *see* claims 1(b) & 2(b). None of these compounds required by the claimed bone replacement material are found in the Berger product.

One of the significant differences is the presence of Q_1 groups of diphosphates ($\text{Na}_7\text{CaP}_2\text{O}_7$, $\text{K}_2\text{CaP}_2\text{O}_7$, $\text{Ca}_2\text{P}_2\text{O}_7$) measured by ^{31}P -MAS-NMR measurements.

Enclosed Fig. 1 of a ^{31}P -MAS-NMR spectra shows peaks of orthophosphates in the δ range of +5 to -2. Further it shows peaks of diphosphates in the δ range of -7.5 to -9.5.

Enclosed Fig. 2 of a ^{31}P -MAS-NMR spectra shows the same situation as in Fig. 1 but with higher diphosphate peaks for comparison. The starting materials for the bone replacement materials evaluated in Fig. 1 and Fig. 2 came from the following raw materials:

Fig. 1 (material of application 10/689,217): CaO 39.86 wt-%, MgO 1.25 wt-%, P_2O_5 46.82 wt-%, Na_2O 4.79 wt-%, K_2O 7.28 wt-%

Fig. 2 (material of application No. 10/689,219): CaO 29.92 wt-%; MgO 2.39 wt-%, P_2O_5 44.53 wt-%, Na_2O 9.19 wt-%; K_2O 13.97 wt-%

The materials used for Fig. 1 and 2 above were prepared according to the method of the present invention with holding steps during the heating procedure at 400, 800 and 1000°C and a melting temperature of 1600°C.

Fig. 3 is a material according to the Berger reference W091/07357, where the starting materials were melted at a temperature of 1550°C and without any holding steps. The material with the following composition: 32.33 wt-% CaO; 1.22 wt-% MgO; 9.4 wt-% Na_2O ; 14.3 wt-%

K₂O; 40.93 wt-% P₂O₅; and 1.82 wt-% SiO₂. The materials produced according to Berger show orthophosphate peaks but no diphosphate peaks using ³¹P-MAS-NMR.

Clearly, Berger does not disclose or suggest the thermal treatment required to form the claimed invention. Because of these divergent thermal treatments, the material from Berger and the material of the claimed invention contain different amounts of crystalline and amorphous phases; crystals with distinct inorganic compounds; and substantially different solubility.

4. In conclusion, it is my opinion that the Berger reference neither discloses nor suggests the claimed bone replacement material or the process of making the claimed bone replacement material. It is also my opinion that the data supplied herein clearly demonstrates that the vitreous or vitreous crystalline, rapidly dissolving materials disclosed in Berger have different crystalline and amorphous phases and include different inorganic compounds than the claims of the Application. Furthermore, the differences in process and end product between Berger and the claims of the Application are not disclosed or suggested by Berger.

5. I further state that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with my knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



Date: This 16th January 2008

Dr. sc. techn. Georg M. Berger

Enclosure: Figs. 1-3

1

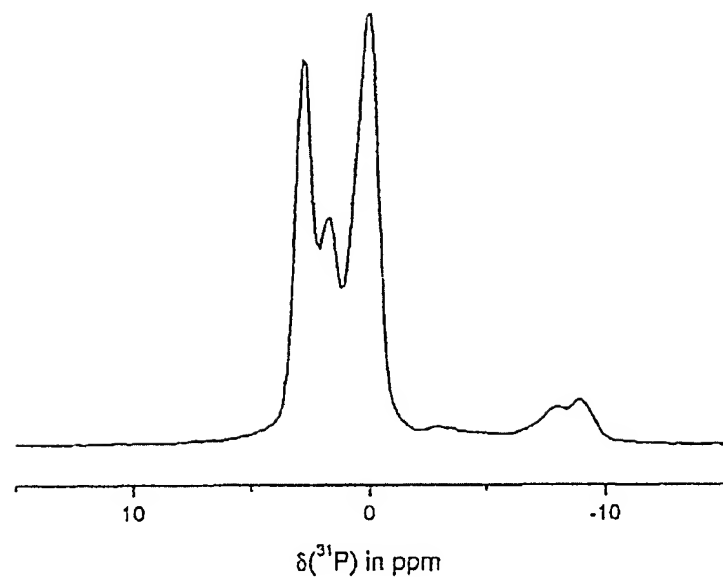


Fig. 1

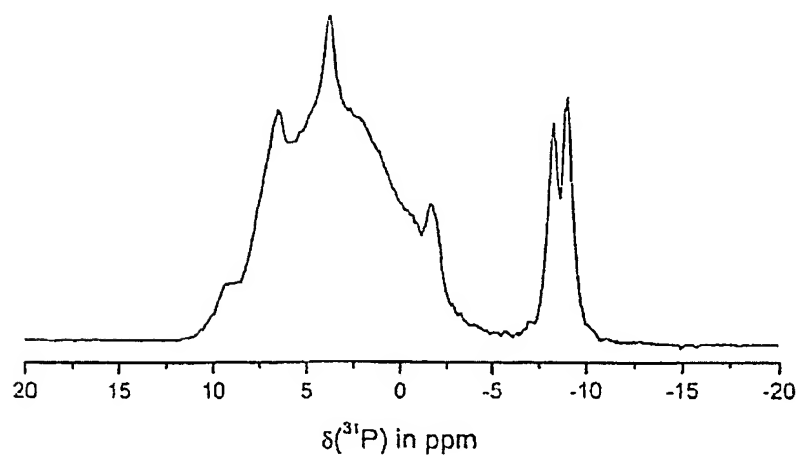


Fig. 2

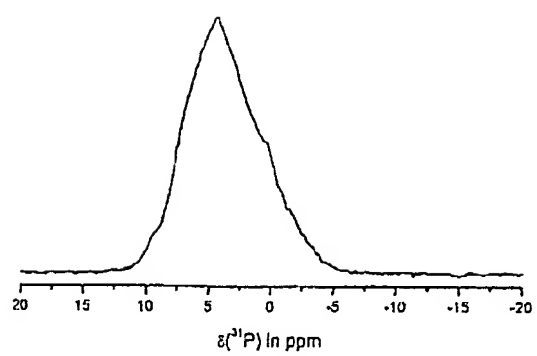


Fig. 3